

**Amendments to the Claims:**

1. (Currently Amended) A method of producing an antibody in the milk of a non-human transgenic mammal, comprising:

providing a transgenic mammal whose somatic and germ cells comprise a sequence encoding an exogenous heavy chain variable region or antigen binding fragment thereof, at least one heavy chain constant region, or a fragment thereof, and a hinge region, operably linked to a promoter which directs expression in mammary epithelial cells, wherein said hinge region has been altered from the hinge region normally associated with the heavy chain constant region[.];

wherein said alteration is the replacement of at least one serine residue with at least one proline residue.
2. (Original) The method of claim 1, wherein at least 70% of the antibodies present in the milk are in assembled form.
3. (Original) The method of claim 1, wherein said transgenic mammal further comprises a sequence encoding a light chain variable region, or antigen binding fragment thereof, and a light chain constant region or functional fragment thereof, operably linked to a promoter which directs expression in mammary epithelial cells.
4. (Currently Amended) The method of claim 1, further comprising the step of obtaining milk from said transgenic mammal, to thereby provide an antibody composition.
5. (Currently Amended) The method of claim 4, further comprising the step of purifying the exogenous antibody from the milk produced by said transgenic mammal.

6. (Currently Amended) The method of claim 1, wherein said promoter is a promoter selected from the group consisting of: casein promoter, lactalbumin promoter, beta lactoglobulin promoter and whey acid protein promoter.

7. (Currently Amended) The method of claim 1, wherein said transgenic mammal is a mammal selected from the group consisting of: cow, goat, mouse rat, sheep, pig and rabbit.

8. (Currently Amended) The method of claim 1, wherein the antibody is an antibody selected from the group consisting of: IgA, IgD, IgM, IgE or IgG.

9. (Currently Amended) The method of claim 1, wherein the antibody is an IgG antibody.

10. (Currently Amended) The method of claim 1, wherein the antibody is an IgG4 antibody.

11. (Currently Amended) The method of claim 10, wherein all or a portion of the hinge region of said antibody has been altered.

12. (Original) The method of claim 10, wherein all or a portion of the hinge region of the antibody has been replaced, e.g. replaced with a hinge region or portion thereof which differs from the hinge region normally associated with said heavy chain constant region.

13. (Original) The method of claim 10, wherein the amino acid sequence of the hinge region of the antibody differs from the amino acid sequence of the hinge region naturally associated with said heavy chain constant region by at least one amino acid residue.

14. (Currently Amended) The method of claim 1, wherein at least one of the nucleic acid residues of the nucleic acid sequence encoding the hinge region of the antibody ~~differs~~

has been removed or changed from the naturally occurring nucleic acid sequence of the hinge region naturally associated with said heavy chain constant region.

15. (Original) The method of claim 12, wherein the hinge region of the antibody, or portion thereof, has been replaced with the hinge region, or portion thereof, of an antibody other than an IgG4 antibody.
16. (Currently Amended) The method of claim 12, wherein the hinge region, or portion thereof, of the antibody has been replaced with a hinge region, or portion thereof, derived from an antibody selected from a group consisting of: IgG1, IgG2 and IgG3.
17. (Currently Amended) The method of claim 12, wherein the hinge region of the antibody, or a portion thereof, has been replaced with a hinge region, or portion thereof, derived from an antibody selected from a group consisting of: IgA, IgD, IgM and IgE.
18. (Currently Amended) The method of claim 12, wherein one or more amino acids of the hinge region have been replaced with [[an]] a different amino acid corresponding to that position in an antibody other than an IgG4 antibody.
19. (Currently Amended) The method of claim 15, wherein the antibody other than an IgG4 antibody is an antibody selected from the group consisting of: IgA, IgD, IgM and IgE.
20. (Currently Amended) The method of claim 15, wherein the antibody other than an IgG4 antibody is an antibody selected from the group consisting of: IgG1, IgG2 and IgG3.
21. (Original) The method of claim 10, wherein a serine residue of the hinge region has been replaced with a proline residue.

22. (Original) The method of claim 10, wherein a serine residue at amino acid number 241 of the hinge region has been replaced with a proline residue.

23. (Original) The method of claim 10, wherein at least one amino acid in the hinge region other than a cysteine residue is replaced with a cysteine residue.

24. (Currently Amended) The method of claim 10, wherein at least 1 glycosylation site of the antibody is altered.

25. (Original) The method of claim 24, wherein at least one glycosylation site in the heavy chain or light chain is altered.

26. (Original) The method of claim 24, wherein at least one glycosylation site in the hinge region of the heavy chain is modified.

27. (Currently Amended) The method of claim 1, wherein the antibody is humanized.

28. (Currently Amended) The method of claim 1, wherein the antibody is chimeric.

29. (Currently Amended) The method of claim 1, wherein the antibody is a human antibody.

30. (Currently Amended) The method of claim 1, wherein the milk of the transgenic mammal is essentially free from a half molecule form of the exogenous antibody.

31. (Currently Amended) The method of claim 1, wherein the ratio of assembled exogenous antibody to half forms of the antibody present in the milk of a transgenic mammal are at least 2:1, 3:1, 4:1 or 5:1.

32. (Currently Amended) A method of producing a non-human transgenic mammal whose somatic and germ cells comprise a modified antibody coding sequence wherein said modified antibody coding sequence encodes an antibody molecule or portion thereof expressible in milk, comprising a modified hinge region, said method comprising the steps of:

introducing into a mammalian cell line a nucleic acid construct comprising a sequence encoding an exogenous heavy chain variable region or antigen binding fragment thereof, at least one heavy chain constant region or a fragment thereof, and a hinge region, operably linked to a promoter which directs expression in mammary epithelial cells, wherein said hinge region has been altered from the hinge region normally associated with the heavy chain constant region[[.]]; and,

introducing said cell into an embryo or microinjecting a construct into an embryo;  
transplanting the embryo into a viable host animal;  
screening for the expression of the desired transgene;  
wherein the alteration made is to eliminate at least one N-linked glycosylation site on the  
CH2 region of an antibody's heavy chain constant region.

33. (Currently Amended) The method of claim [[33]] 32, wherein said hinge region has been altered such that at least 70% of the exogenous antibodies present in the milk of the transgenic mammal are in assembled form.

34. (Original) The method of claim 33, wherein said modified antibody coding sequence further comprises a sequence encoding a light chain variable region or antigen binding fragment

thereof and a light chain constant region or functional fragment thereof, operably linked to a promoter which directs expression in mammary epithelial cells.

35. (Currently Amended) The method of claim 33, wherein the promoter is a promoter selected from the group consisting of: casein promoter, lactalbumin promoter, beta lactoglobulin promoter and whey acid protein promoter.

36. (Currently Amended) The method of claim 33, wherein the transgenic mammal is a mammal selected from the group consisting of: cow, goat, mouse rat, sheep, pig and rabbit.

37. (Currently Amended) The method of claim 33, wherein the antibody is an antibody selected from the group consisting of: IgA, IgD, IgM, IgE or IgG.

38. (Currently Amended) The method of claim 33, wherein the antibody is an IgG antibody.

39. (Currently Amended) The method of claim 33, wherein the antibody is an IgG4 antibody.

40. (Currently Amended) The method of claim [40]] 32, wherein all or a portion of the hinge region of the antibody has been altered.

41. (Currently Amended) The method of claim 40, wherein all or a portion of the hinge region of the antibody has been replaced, e.g. replaced with a hinge region or portion thereof which differs from the hinge region normally associated with said heavy chain variable region or said constant region.

42. (Original) The method of claim 40, wherein the amino acid sequence of the hinge region of the antibody differs from the amino acid sequence of the hinge region naturally associated with said heavy chain constant region by at least one amino acid residue.

43. (Original) The method of claim 33, wherein at least one of the nucleic acid residues of the nucleic acid sequence encoding the hinge region of the antibody differs from the nucleic acid sequence of the hinge region naturally associated with said heavy chain constant region.

44. (Currently Amended) The method of claim [[44]] 40, wherein the hinge region of the antibody, or portion thereof, has been replaced with the hinge region, or portion thereof, of an antibody other than an IgG4 antibody.

45. (Currently Amended) The method of claim 42, wherein the hinge region, or portion thereof, of the antibody has been replaced with a hinge region, or portion thereof, derived from an antibody selected from a group consisting of: IgG1, IgG2 and IgG3.

46. (Currently Amended) The method of claim 42, wherein the hinge region of the antibody, or a portion thereof, has been replaced with a hinge region, or portion thereof, derived from an antibody selected from a group consisting of: IgA, IgD, IgM and IgE.

47. (Currently Amended) The method of claim 42, wherein one or more amino acids of the hinge region have been replaced with an amino acid corresponding to that position in an antibody other than an IgG4 antibody.

48. (Currently Amended) The method of claim [[48]] 44, wherein the antibody other than an IgG4 antibody is an antibody selected from the group consisting of: IgA, IgD, IgM and IgE.

49. (Currently Amended) The method of claim 48, wherein the antibody other than an IgG4 antibody is an antibody selected from the group consisting of: IgG1, IgG2 and IgG3.

50. (Original) The method of claim 40, wherein a serine residue of the hinge region has been replaced with a proline residue.

51. (Original) The method of claim 40, wherein a serine residue at amino acid number 241 of the hinge region has been replaced with a proline residue.

52. (Original) The method of claim 40, wherein at least one amino acid in the hinge region other than a cysteine residue is replaced with a cysteine residue.

53. (Currently Amended) The method of claim 40, wherein at least one glycosylation site of the antibody is altered.

54. (Currently Amended) The method of claim 54, wherein at least one glycosylation site in the heavy chain or light chain is altered.

55. (Original) The method of claim 40, wherein at least one glycosylation site in the hinge region of the heavy chain is modified.

56. (Currently Amended) The method of claim 33, wherein the antibody is humanized.

57. (Currently Amended) The method of claim 33, wherein the antibody is a human antibody.

58. (Currently Amended) The method of claim 33, wherein the antibody is chimeric.

59. (Original) The method of claim 33, wherein said hinge region has been altered such that the milk of the transgenic mammal is essentially free from a half molecule form of the exogenous antibody.

60. (Currently Amended) The method of claim 33, wherein the ratio of assembled exogenous antibody to half forms of the antibody present in the milk of a transgenic mammal are at least 2:1, 3:1, 4:1 or 5:1.

61. (Currently Amended) The method of claim 60, wherein the antibody is an antibody selected from the group consisting of: IgA, IgD, IgM, IgE or IgG

62. (Currently Amended) A method of producing a non-human transgenic mammal capable of expressing an assembled exogenous antibody or portion thereof in its milk, the method comprising:

introducing into a mammal a construct comprising a sequence encoding a light chain of exogenous antibody operably linked to a promoter which directs expression in mammary epithelial cells; and

introducing into the mammal a nucleic acid construct comprising a sequence encoding a mutagenized heavy chain of the exogenous antibody or a portion thereof operably linked to a promoter which directs expression in mammary epithelial cells, wherein the heavy chain or portion thereof comprises a hinge region which has been altered such that at least 70% of the exogenous antibodies present in the milk are in assembled form[. . .]; and,

introducing said cell into an embryo or microinjecting a construct into an embryo;  
transplanting the embryo into a viable host animal;  
screening for the expression of the desired transgene;

wherein at least one amino acid residue present in the hinge region of an Ig molecule has been replaced with a cysteine residue.

63. (Currently Amended) A method of producing a non-human transgenic mammal capable of expressing an assembled exogenous antibody in its milk, the method comprising: providing a cell from a transgenic mammal whose germ and somatic cells comprise a sequence encoding a light chain of an exogenous antibody operably linked to a promoter which directs expression in mammary epithelial cells; and introducing into the cell a nucleic acid construct comprising a sequence encoding a mutagenized heavy chain of the exogenous antibody or a portion thereof operably linked to a promoter which directs expression in mammary epithelial cells, wherein the heavy chain, or portion thereof comprises a hinge region which has been altered such that at least 70% of the exogenous antibodies present in the milk are in assembled form[[.]]; and, introducing said cell into an embryo or microinjecting a construct into an embryo; transplanting the embryo into a viable host animal; screening for the expression of the desired transgene; wherein the entire hinge region of a first Ig molecule has been replaced with the hinge region of a second Ig molecule.

64-89. (Cancelled)

90. (New) The method of claim 1, wherein said at least one serine residue replaced with a proline residue is serine 241 in an IgG4 antibody are in assembled form.

91. (New) The method of claim 32, wherein said alteration made to eliminate at least one N-linked glycosylation site on the CH2 region of an antibody's heavy chain constant region

is an alteration that eliminates an N-linked glycosylation site on the CH2 of an IgG heavy chain by replacing an asparagine residue to a glutamine residue at the consensus site.

92. (New) The method of claim 63 wherein the entire hinge region of a first IgG4 molecule has been replaced with the hinge region of a second IgG molecule